

647 04



OIEP

ENTERED #8

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/903,323A

DATE: 03/18/2002

TIME: 15:36:32

Input Set : A:\510015-261.TXT

Output Set: N:\CRF3\03182002\I903323A.raw

4 <110> APPLICANT: De Robertis, Edward M.
 5 Bouwmeester, Tewis
 8 <120> TITLE OF INVENTION: Endoderm, Cardiac and Neural Inducing
 9 Factors
 11 <130> FILE REFERENCE: 510015-261
 13 <140> CURRENT APPLICATION NUMBER: US 09/903,323A
 14 <141> CURRENT FILING DATE: 2001-07-11
 16 <150> PRIOR APPLICATION NUMBER: US 60/020,150
 17 <151> PRIOR FILING DATE: 1996-06-20
 19 <160> NUMBER OF SEQ ID NOS: 10
 21 <170> SOFTWARE: FastSEQ for Windows Version 3.0
 23 <210> SEQ ID NO: 1
 24 <211> LENGTH: 270
 25 <212> TYPE: PRT
 26 <213> ORGANISM: Xenopus
 28 <400> SEQUENCE: 1
 29 Met Leu Leu Asn Val Leu Arg Ile Cys Ile Ile Val Cys Leu Val Asn
 30 1 5 10 15
 31 Asp Gly Ala Gly Lys His Ser Glu Gly Arg Glu Arg Thr Lys Thr Tyr
 32 20 25 30
 33 Ser Leu Asn Ser Arg Gly Tyr Phe Arg Lys Glu Arg Gly Ala Arg Arg
 34 35 40 45
 35 Ser Lys Ile Leu Leu Val Asn Thr Lys Gly Leu Asp Glu Pro His Ile
 36 50 55 60
 37 Gly His Gly Asp Phe Gly Leu Val Ala Glu Leu Phe Asp Ser Thr Arg
 38 65 70 75 80
 39 Thr His Thr Asn Arg Lys Glu Pro Asp Met Asn Lys Val Lys Leu Phe
 40 85 90 95
 41 Ser Thr Val Ala His Gly Asn Lys Ser Ala Arg Arg Lys Ala Tyr Asn
 42 100 105 110
 43 Gly Ser Arg Arg Asn Ile Phe Ser Arg Arg Ser Phe Asp Lys Arg Asn
 44 115 120 125
 45 Thr Glu Val Thr Glu Lys Pro Gly Ala Lys Met Phe Trp Asn Asn Phe
 46 130 135 140
 47 Leu Val Lys Met Asn Gly Ala Pro Gln Asn Thr Ser His Gly Ser Lys
 48 145 150 155 160
 49 Ala Gln Glu Ile Met Lys Glu Ala Cys Lys Thr Leu Pro Phe Thr Gln
 50 165 170 175
 51 Asn Ile Val His Glu Asn Cys Asp Arg Met Val Ile Gln Asn Asn Leu
 52 180 185 190
 53 Cys Phe Gly Lys Cys Ile Ser Leu His Val Pro Asn Gln Gln Asp Arg
 54 195 200 205
 55 Arg Asn Thr Cys Ser His Cys Leu Pro Ser Lys Phe Thr Leu Asn His

RECEIVED
 APR 18 2002
 TECH CENTER 1600/2900

RAW SEQUENCE LISTING

DATE: 03/18/2002

PATENT APPLICATION: US/09/903,323A

TIME: 15:36:32

Input Set : A:\510015-261.TXT

Output Set: N:\CRF3\03182002\I903323A.raw

```

56          210          215          220
57 Leu Thr Leu Asn Cys Thr Gly Ser Lys Asn Val Val Lys Val Val Met
58 225          230          235          240
59 Met Val Glu Glu Cys Thr Cys Glu Ala His Lys Ser Asn Phe His Gln
60          245          250          255
61 Thr Ala Gln Phe Asn Met Asp Thr Ser Thr Thr Leu His His
62          260          265          270
64 <210> SEQ ID NO: 2
65 <211> LENGTH: 1338
66 <212> TYPE: DNA
67 <213> ORGANISM: Xenopus
69 <400> SEQUENCE: 2
70 gaattccag caagtcgctc agaaacactg cagggctctag atatcataca atgttactaa 60
71 atgtactcag gatctgtatt atcgtctgcc ttgtgaatga tggagcagga aaacactcag 120
72 aaggacgaga aaggacaaaa acatattcac ttaacagcag aggttacttc agaaaagaaa 180
73 gaggagcacg taggagcaag attctgctgg tgaatactaa aggtcttgat gaacccaca 240
74 ttgggcatgg tgattttcgc ttagtagctg aactatttga ttccaccaga acacatacaa 300
75 acagaaaaga gccagacatg aacaaagtca agcttttctc aacagttgcc catggaaca 360
76 aaagtgcaag aagaaaagct tacaatgggt ctagaaggaa tatttttctc cgccgttctt 420
77 ttgataaaag aaatacacag gttactgaaa agcctgggtg caagatgttc tggaacaatt 480
78 ttttggttaa aatgaatgga gccccacaga atacaagcca tggcagtaaa gcacaggaaa 540
79 taatgaaaga agcttgcaaa accttgtttt tcaactcagaa tattgtacat gaaaactgtg 600
80 acaggatggt gatacagaac aatctgtgct ttggtaaatg catctctctc catgttccaa 660
81 atcagcaaga tcgacgaaat acttgttccc attgcttgcc gtccaaattt accctgaacc 720
82 acctgacgct gaattgtact ggatctaaga atgtagtaaa ggttgctcat atggtagagg 780
83 aatgcacgtg tgaagctcat aagagcaact tccaccaaac tgcacagttt aacatggata 840
84 catctactac cctgcaccat taaaggactg ccatacagta tggaaatgcc cttttgttgg 900
85 aatatttggt acatactatg catctaaagc attatgttgc cttctatttc atataaccac 960
86 atggaataag gattgtatga attataatta acaaatggca ttttgtgtaa catgcaagat 1020
87 ctctgttcca tcagttgcaa gataaaaggc aatatttggt tgactttttt tctacaaaat 1080
88 gaatacccaa atatatgata agataatggg gtcaaaactg ttaaggggta atgtaataat 1140
89 agggactaag tttgccaggg agcagtgacc cataacaacc aatcagcagg tatgatttac 1200
90 tggtcacctg tttaaaagca aacatcttat tggttgctat gggttactgc ttctgggcaa 1260
91 aatgtgtgcc tcataggggg gttagtgtgt tgtgtactga ataatgtga tttatttcat 1320
92 tgttacaaaa aaaaaaaaaa 1338
94 <210> SEQ ID NO: 3
95 <211> LENGTH: 318
96 <212> TYPE: PRT
97 <213> ORGANISM: Xenopus frazzled
99 <400> SEQUENCE: 3
100 Met Ser Arg Thr Arg Lys Val Asp Ser Leu Leu Leu Leu Ala Ile Pro
101 1          5          10          15
102 Gly Leu Ala Leu Leu Leu Leu Pro Asn Ala Tyr Cys Ala Ser Cys Glu
103          20          25          30
104 Pro Val Arg Ile Pro Met Cys Lys Ser Met Pro Trp Asn Met Thr Lys
105          35          40          45
106 Met Pro Asn His Leu His His Ser Thr Gln Ala Asn Ala Ile Leu Ala
107          50          55          60
108 Ile Glu Gln Phe Glu Gly Leu Leu Thr Thr Glu Cys Ser Gln Asp Leu

```

RAW SEQUENCE LISTING
PATENT APPLICATION: US/09/903,323A

DATE: 03/18/2002
TIME: 15:36:32

Input Set : A:\510015-261.TXT
Output Set: N:\CRF3\03182002\I903323A.raw

```

109 65          70          75          80
110 Leu Phe Phe Leu Cys Ala Met Tyr Ala Pro Ile Cys Thr Ile Asp Phe
111          85          90          95
112 Gln His Glu Pro Ile Lys Pro Cys Lys Ser Val Cys Glu Arg Ala Arg
113          100          105          110
114 Ala Gly Cys Glu Pro Ile Leu Ile Lys Tyr Arg His Thr Trp Pro Glu
115          115          120          125
116 Ser Leu Ala Cys Glu Glu Leu Pro Val Tyr Asp Arg Gly Val Cys Ile
117          130          135          140
118 Ser Pro Glu Ala Ile Val Thr Val Glu Gln Gly Thr Asp Ser Met Pro
119          145          150          155          160
120 Asp Phe Ser Met Asp Ser Asn Asn Gly Asn Cys Gly Ser Gly Arg Glu
121          165          170          175
122 His Cys Lys Cys Lys Pro Met Lys Ala Thr Gln Lys Thr Tyr Leu Lys
123          180          185          190
124 Asn Asn Tyr Asn Tyr Val Ile Arg Ala Lys Val Lys Glu Val Lys Val
125          195          200          205
126 Lys Cys His Asp Ala Thr Ala Ile Val Glu Val Lys Glu Ile Leu Lys
127          210          215          220
128 Ser Ser Leu Val Asn Ile Pro Lys Asp Thr Val Thr Leu Tyr Thr Asn
129          225          230          235          240
130 Ser Gly Cys Leu Cys Pro Gln Leu Val Ala Asn Glu Glu Tyr Ile Ile
131          245          250          255
132 Met Gly Tyr Glu Asp Lys Glu Arg Thr Arg Leu Leu Leu Val Glu Gly
133          260          265          270
134 Ser Leu Ala Glu Lys Trp Arg Asp Arg Leu Ala Lys Lys Val Lys Arg
135          275          280          285
136 Trp Asp Gln Lys Leu Arg Arg Pro Arg Lys Ser Lys Asp Pro Val Ala
137          290          295          300
138 Pro Ile Pro Asn Lys Asn Ser Asn Ser Arg Gln Ala Arg Ser
139          305          310          315
141 <210> SEQ ID NO: 4
142 <211> LENGTH: 1875
143 <212> TYPE: DNA
144 <213> ORGANISM: Xenopus frazzled
146 <400> SEQUENCE: 4
147 gaattccctt tcacacagga ctccctggcag aggtgaatgg ttagccctat ggatttggtt 60
148 tgttgatttt gacacatgat tgattgcttt cagataggat tgaaggactt ggatttttat 120
149 ctaattctgc acttttaaat tatctgagta attgttcatt ttgtattgga tgggactaaa 180
150 gataaactta actccttgct ttgacttgcc ccataaacta taagggtggg tgagttgtag 240
151 ttgcttttac atgtgccag attttccctg tattccctgt attccctcta aagtaagcct 300
152 acacatacag gttgggcaga ataacaatgt ctogaacaag gaaagtggac tcattactgc 360
153 tactggccat acctggactg gcgcttctct tattacccaa tgcttactgt gcttcgtgtg 420
154 agcctgtgcg gatcccatg tgcaaatcta tgccatggaa catgaccaag atgcccaacc 480
155 atctccacca cagcactcaa gccaatgcca tcctggcaat tgaacagttt gaaggtttgc 540
156 tgaccactga atgtagccag gaccttttgt tctttctgtg tgccatgtat gcccccattt 600
157 gtaccatcga ttccagcat gaaccaatta agccttgcaa gtccgtgtgc gaaagggcca 660
158 gggccggtg tgagccatt ctcataaagt accggcacac ttggccagag agcctggcat 720
159 gtgaagagct gcccgatat gacagaggag tctgcatctc ccagaggct atcgtcacag 780

```

RAW SEQUENCE LISTING
PATENT APPLICATION: US/09/903,323A

DATE: 03/18/2002
TIME: 15:36:32

Input Set : A:\510015-261.TXT
Output Set: N:\CRF3\03182002\I903323A.raw

```

160  tggaaacaagg aacagattca atgccagact tctccatgga ttcaaacaat ggaaattgcg      840
161  gaagcggcag  ggagcactgt aaatgcaagc ccatgaaggc aacccaaaag acgtatctca      900
162  agaataatta caattatgta atcagagcaa aagtgaaga ggtgaaagtg aaatgccacg      960
163  acgcaacagc aattgtggaa gtaaaggaga ttctcaagtc ttccctagtg aacattccta     1020
164  aagacacagt gacactgtac accaactcag gctgcttggt cccccagctt gttgccaatg     1080
165  aggaatacat aattatgggc tatgaagaca aagagcgtac caggcttcta ctagtggaag     1140
166  gatccttggc cgaaaaatgg agagatcgtc ttgctaagaa agtcaagcgc tgggatcaaa     1200
167  agcttcgacg tcccaggaaa agcaaagacc ccgtggctcc aattcccaac aaaaacagca     1260
168  attccagaca agcgcgtagt tagactaacg gaaagggtga tggaaactct atggactttg     1320
169  aaactaagat ttgcattgtt ggaagagcaa aaaagaaatt gcactacagc acgttatatt     1380
170  ctattgttta ctacaagaag ctggtttagt tgattgtagt tctcctttcc ttcttttttt     1440
171  ttataactat attgcacgt gttcccaggc aattgtttta ttcaacttcc agtgacagag     1500
172  cagtgactga atgtctcagc ctaaagaagc tcaattcatt tctgatcaac taatggtgac     1560
173  aagtgtttga tacttgggga aagtgaacta attgcaatg taaatcagag aaaagttgac     1620
174  caatgttgct tttccgttag atgaacaagt gagagatcac atttaaatga tgatcacttt     1680
175  ccatttaata ctttcagcag ttttagttag atgacatgta ggatgcacct aaatctaaat     1740
176  attttatcat aaatgaagag ctggtttaga ctgtatggtc actgttggtg aggtaaatgc     1800
177  ctactttgtc aattctgttt taaaaattgc ctaataaat attagtcctt aaataaaaaa     1860
178  aaaaaaaaaa aaaaaa                                     1875
180 <210> SEQ ID NO: 5
181 <211> LENGTH: 896
182 <212> TYPE: PRT
183 <213> ORGANISM: Xenopus
185 <400> SEQUENCE: 5
186  Met Leu Leu Leu Phe Arg Ala Ile Pro Met Leu Leu Leu Gly Leu Met
187      1          5          10          15
188  Val Leu Gln Thr Asp Cys Glu Ile Ala Gln Tyr Tyr Ile Asp Glu Glu
189      20          25          30
190  Glu Pro Pro Gly Thr Val Ile Ala Val Leu Ser Gln His Ser Ile Phe
191      35          40          45
192  Asn Thr Thr Asp Ile Pro Ala Thr Asn Phe Arg Leu Met Lys Gln Phe
193      50          55          60
194  Asn Asn Ser Leu Ile Gly Val Arg Glu Ser Asp Gly Gln Leu Ser Ile
195      65          70          75          80
196  Met Glu Arg Ile Asp Arg Glu Gln Ile Cys Arg Gln Ser Leu His Cys
197      85          90          95
198  Asn Leu Ala Leu Asp Val Val Ser Phe Ser Lys Gly His Phe Lys Leu
199      100         105         110
200  Leu Asn Val Lys Val Glu Val Arg Asp Ile Asn Asp His Ser Pro His
201      115         120         125
202  Phe Pro Ser Glu Ile Met His Val Glu Val Ser Glu Ser Ser Ser Val
203      130         135         140
204  Gly Thr Arg Ile Pro Leu Glu Ile Ala Ile Asp Glu Asp Val Gly Ser
205      145         150         155         160
206  Asn Ser Ile Gln Asn Phe Gln Ile Ser Asn Asn Ser His Phe Ser Ile
207      165         170         175
208  Asp Val Leu Thr Arg Ala Asp Gly Val Lys Tyr Ala Asp Leu Val Leu
209      180         185         190
210  Met Arg Glu Leu Asp Arg Glu Ile Gln Pro Thr Tyr Ile Met Glu Leu

```

RAW SEQUENCE LISTING
 PATENT APPLICATION: US/09/903,323A

DATE: 03/18/2002
 TIME: 15:36:32

Input Set : A:\510015-261.TXT
 Output Set: N:\CRF3\03182002\I903323A.raw

211	195	200	205
212	Leu Ala Met Asp Gly Gly Val Pro Ser Leu Ser Gly Thr Ala Val Val		
213	210	215	220
214	Asn Ile Arg Val Leu Asp Phe Asn Asp Asn Ser Pro Val Phe Glu Arg		240
215	225	230	235
216	Ser Thr Ile Ala Val Asp Leu Val Glu Asp Ala Pro Leu Gly Tyr Leu		255
217	245	250	255
218	Leu Leu Glu Leu His Ala Thr Asp Asp Asp Glu Gly Val Asn Gly Glu		270
219	260	265	270
220	Ile Val Tyr Gly Phe Ser Thr Leu Ala Ser Gln Glu Val Arg Gln Leu		285
221	275	280	285
222	Phe Lys Ile Asn Ser Arg Thr Gly Ser Val Thr Leu Glu Gly Gln Val		300
223	290	295	300
224	Asp Phe Glu Thr Lys Gln Thr Tyr Glu Phe Glu Val Gln Ala Gln Asp		320
225	305	310	315
226	Leu Gly Pro Asn Pro Leu Thr Ala Thr Cys Lys Val Thr Val His Ile		335
227	325	330	335
228	Leu Asp Val Asn Asp Asn Thr Pro Ala Ile Thr Ile Thr Pro Leu Thr		350
229	340	345	350
230	Thr Val Asn Ala Gly Val Ala Tyr Ile Pro Glu Thr Ala Thr Lys Glu		365
231	355	360	365
232	Asn Phe Ile Ala Leu Ile Ser Thr Thr Asp Arg Ala Ser Gly Ser Asn		380
233	370	375	380
234	Gly Gln Val Arg Cys Thr Leu Tyr Gly His Glu His Phe Lys Leu Gln		400
235	385	390	395
236	Gln Ala Tyr Glu Asp Ser Tyr Met Ile Val Thr Thr Ser Thr Leu Asp		415
237	405	410	415
238	Arg Glu Asn Ile Ala Ala Tyr Ser Leu Thr Val Val Ala Glu Asp Leu		430
239	420	425	430
240	Gly Phe Pro Ser Leu Lys Thr Lys Lys Tyr Tyr Thr Val Lys Val Ser		445
241	435	440	445
242	Asp Glu Asn Asp Asn Ala Pro Val Phe Ser Lys Pro Gln Tyr Glu Ala		460
243	450	455	460
244	Ser Ile Leu Glu Asn Asn Ala Pro Gly Ser Tyr Ile Thr Thr Val Ile		480
245	465	470	475
246	Ala Arg Asp Ser Asp Ser Asp Gln Asn Gly Lys Val Asn Tyr Arg Leu		495
247	485	490	495
248	Val Asp Ala Lys Val Met Gly Gln Ser Leu Thr Thr Phe Val Ser Leu		510
249	500	505	510
250	Asp Ala Asp Ser Gly Val Leu Arg Ala Val Arg Ser Leu Asp Tyr Glu		525
251	515	520	525
252	Lys Leu Lys Gln Leu Asp Phe Glu Ile Glu Ala Ala Asp Asn Gly Ile		540
253	530	535	540
254	Pro Gln Leu Ser Thr Arg Val Gln Leu Asn Leu Arg Ile Val Asp Gln		560
255	545	550	555
256	Asn Asp Asn Cys Pro Val Ile Thr Asn Pro Leu Leu Asn Asn Gly Ser		575
257	565	570	575
258	Gly Glu Val Leu Leu Pro Ile Ser Ala Pro Gln Asn Tyr Leu Val Phe		590
259	580	585	590

VERIFICATION SUMMARY

PATENT APPLICATION: US/09/903,323A

DATE: 03/18/2002
TIME: 15:36:33

Input Set : A:\510015-261.TXT

Output Set: N:\CRF3\03182002\I903323A.raw